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EFFECTS ON BLOOD PRESSURE AND HEART RATE OF SELECTIVE SHIELDING OF MIDLINE TRUNK STRUCTURES IN MONKEYS EXPOSED TO 1000 RADS ^{60}Co

Lovelace Foundation
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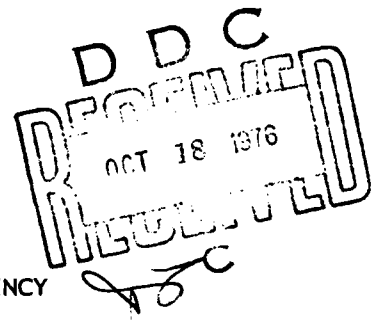

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Blood pressure (BP) and heart rate (HR) were monitored in three groups of shielded, nonperforming monkeys, and one unshielded control during and after exposure to 1000 rads ^{60}Co at 150 rad/min. A narrow, vertically-oriented lead shield was located over either the dorsal midline (vertebral column) or laterally just to the left or right of midline in the three shielding groups. Purpose was to determine if selective

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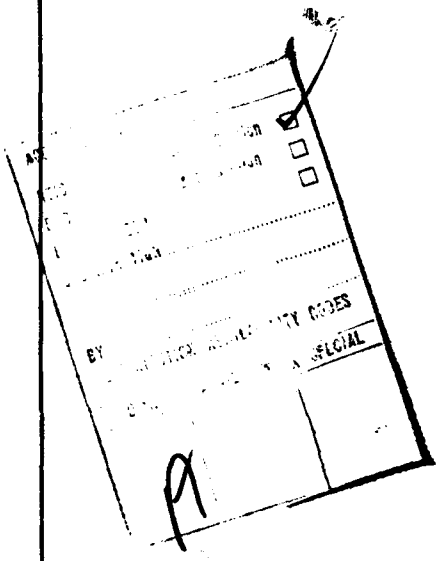
shielding of underlying structures (e.g., spinal cord, autonomic ganglia, heart, spleen, etc.) would alter the postradiation hypotensive response. No differential effects of shielding placement on BP or HR were observed, nor did the shielding groups differ from the unshielded. Absence of radiosensitive target organs implies the hypotensive trigger site is diffuse, for example, the peripheral vasculature.



PREFACE

This work was performed as a Nuclear Weapons Effects Subtask entitled "Neurophysiological Basis of Primate Performance Decrement," funded by the Defense Nuclear Agency under Contract No. DASA-01-70-C-0059 and DNA-001-74-C-0098. The present report found no evidence for radiosensitive target organs or systems mediating the postradiation hypotensive response in monkeys using a selective shielding method. The target sites for hypotension and presumably performance decrement are probably diffuse, for example, the peripheral vasculature.

The author thanks the following individuals for their contributions: E. A. Henderson, C. D. Campbell, A. W. Neely, V. Bogo, and R. L. Powis.

This research was conducted according to the principles enunciated in the "Guide for Laboratory Animal Facilities and Care," prepared by the National Academy of Sciences, National Research Council.

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INTRODUCTION

In their attempts to localize a target organ or system responsible for the early postradiation hypotension/performance decrement syndrome shown by monkeys, previous studies have conducted experiments employing partial-body shielding to selectively irradiate the head, trunk, or whole body. The effects of head vs trunk exposure on performance measures have been somewhat equivocal, whereas the effects on blood pressure have been fairly consistent.

Thorp and Young[1] found no differential behavioral effects of head or trunk shielding or no shielding in monkeys exposed to either a 2500 or a 10,000 rad TRIGA-reactor pulse while performing a simple shock-avoidance task. All unshielded and many shielded animals exhibited performance decrement to some degree. Strangely, only at 4500 rad did their head- and trunk-shielded groups show less impairment than the unshielded controls, although the 4500-rad head and trunk groups were not significantly different from one another. A source of error noted by the authors was that a dose gradient existed between shielded and unshielded body parts due to incomplete collimation of the mixed gamma-neutron radiation employed.

Chapman and Hurst[2] compared head vs. trunk irradiation in monkeys receiving continuous X-radiation at 280 rad/min for up to 18,000 rads while performing an avoidance task. Performance decrement was first seen in the trunk-exposed animals beginning after receipt of 2340 rads. But no impairment was visible in the head-exposed animals before 11,570 rads had been delivered.

Chapman and Young[3] observed severe, early performance decrement in 4 of 8 monkeys head-exposed to a 6250-rad reactor pulse. The remaining four showed minimum or no such changes. Five of seven trunk-exposed monkeys showed decrement which was generally less severe than in either the head or whole-body radiation groups, the latter group showing the most severe effects of all. All of the trunk-exposed animals showed hypotension to a degree indistinguishable from that of the unshielded subjects. Only two of the eight head-exposed monkeys showed any pronounced early hypotension.

At the high dose (6250 rad) Chapman and Young[3] administered the shielding employed still allowed delivery of 400-500 rad to the shielded body parts. We have demonstrated both significant hypotension[4] and performance decrement[4,5] after such doses of ^{60}Co to unshielded monkeys, so the shielding effects noted by Chapman and Young are unclear

except in demonstrating that the hypotensive response seems to be trunk-mediated.

Chapman[6] compared trunk and whole-body X-irradiation effects (at 200 rad/min) on avoidance behavior and blood pressure and found no between-group differences until 10,000 rads had been absorbed. At that time the whole-body group began showing signs of neurological damage (e.g., increasing muscular incoordination, vertical nystagmus, titubation, and reluctance to move spontaneously leading to complete immobilization in an opisthotonic posture). Such CNS symptoms seem to appear most readily with very high-dose exposures (10,000+ rads) involving the head, and may be prevented by head-shielding in monkeys,[2,6] dogs,[7] and miniature pigs.[8]

To review, the early postradiation hypotension and performance impairments shown by monkeys in the supralethal exposure range below several thousand rads appear to be more readily elicited by trunk or whole-body exposure than head-exposure. Head-only exposure with approximately 6000+ rads tends to elicit primarily CNS impairment but little hypotension. To examine further within the trunk for a zone of differential radiation sensitivity, the present study compared the effects on blood pressure and heart rate of three different placements of a narrow, vertically-oriented shield

situated over the dorsal midline or to either side of same. The object was to selectively shield either: (1) the midline neural structures primarily, (2) the greater portion of the heart and spleen which lie chiefly slightly left of the dorsal midline, or (3) structures lying to the right of dorsal midline; using three separate groups of nonperforming monkeys.

METHOD

Subjects

The subjects were 39 male, rhesus monkeys (Macaca mulatta), weighing between 2 and 3 kg, obtained from Primate Imports Corp., New York. They were treated as necessary for enteric disorders and tuberculin tested during quarantine before entering the experiment.

Apparatus

One week prior to irradiation each subject underwent surgical implantation of a femoral artery polyethylene catheter, performed under halothane general anesthesia following premedication with phencyclidine and atropine. The catheter was inserted into the left femoral artery up to the level of the diaphragm for the recording of systemic arterial blood pressure within the abdominal aorta. The catheter terminated

outside the leg in a three-way Leur-lock fitting secured to the restraining chair near the exit of the catheter at mid-thigh level. The catheter was maintained patent outside the recording periods by pulsed infusion of heparinized saline (5 U./cc/15 min).* Horizontal stocks at the neck and waist levels of the restraining chair as well as a snug-fitting nylon mesh vest prevented the monkey from reaching the catheters. The chair and head-restraint device employed are pictured in Bruner et al.[9]

Blood pressure was recorded with a Kulite pressure transducer** attached to the Leur-lock fitting, and was written out along with tachographically-derived heart rate on a Grass Model 78 Polygraph. Blood pressure was calculated by taking one-third the pulse pressure difference plus the diastolic pressure with reference to atmospheric pressure zero, corrected for transducer distance below the aortic arch.

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* Model 1302, Lambda Pump, Harvard Apparatus Co., 150 Dover Rd., Millis, MA 02054.

** Model PSL 125-6, Kulite Semiconductor Prod., 1039 Hoyt Ave., Ridgefield, NJ 07657.

Procedure

The monkeys were irradiated individually, dorsoventrally while seated in the restraining chair. Fifteen animals were exposed whole-body with no shielding to serve as controls. These animals were also used for other experiments involving some blood sampling or other monitoring which were not considered to affect the present measurements. A lead shield (2.54 cm wide x 4.13 cm thick x 35.56 cm long) was attached to the back of the chair in one of three positions for the left side, midline and right side shield groups, respectively. The shield was designed to allow penetration of less than 8% of the radiation to the midtissue level of the covered parts. Vertically the shield extended below the buttocks and above the head in the seated position. The 2.54-cm-wide dimension was chosen after X-radiography indicated that such was sufficient to adequately cover the vertebral column and its processes for the midline-shield group (n = 8). Radiography also indicated that most of the heart and spleen were protected when the left-side shield position (n = 8) was used. Both the vertebral column and the heart and spleen were exposed when the right-side shield (n = 8) was in place. The left- and right-side shield locations, respectively, began at the left and right edges of the midline shield location.

All animals received 1000 rads ^{60}Co midtissue dose to the exposed portions at a dose rate of 150 rad/min. The exposure was administered in the morning approximately 16 hr after the last feeding. Remoted polygraph recordings of the cardiovascular responses were instituted about 30 min prior to the exposure's start and continued without interruption by the exposure normally to 30 min or more postexposure. All references to postexposure changes are with respect to the time of the exposure's start and thus may have occurred while the exposure, the duration of which was 6.67 min, was still in progress. Dosimetry was determined using high-sensitivity Lithium Flouride Thermoluminescent dosimeters with live and cadaver monkeys and cardboard phantoms. Further details of the exposure and dosimetry may be found in Bruner et al.[9]

RESULTS

Figure 1 presents each group's mean percentage of preradiation baseline for mean blood pressure (BP) and heart rate (HR) for the initial 30 min postexposure. All groups showed hypotension developing after 3 minutes of exposure. The deepest point of hypotension ranged from 79% of preradiation value at 7 min post for the left-side shield

group to 67% at 9 min for the right-side group. All groups showed similar BP recovery curves with BP stabilizing at slightly subnormal levels about 20 min post.

Tachycardia developed for all groups after the third minute of exposure and peaked at about 6 min post. HR then declined to somewhat elevated levels by the final observations. No further important changes occurred in BP or HR beyond 30 min post. Although some intergroup differences are suggested by comparison of the curves in Figure 1, for example for HR between the midline and right-side shield groups, no significant differences whatsoever were obtained among (ANOVA) or between (*t* tests) groups for either BP or HR at any time postirradiation. The standard deviations of the several groups were also of comparable magnitude and showed similar changes over the course of the experiment.

DISCUSSION

The present lack of significant group differences in BP or HR as a function of shielding placement or no shielding implies the absence of any differential radiation sensitivity or mediational qualities for the hypotensive syndrome among the anatomical loci selectively protected and exposed. Thus such structures as heart, spleen, spinal

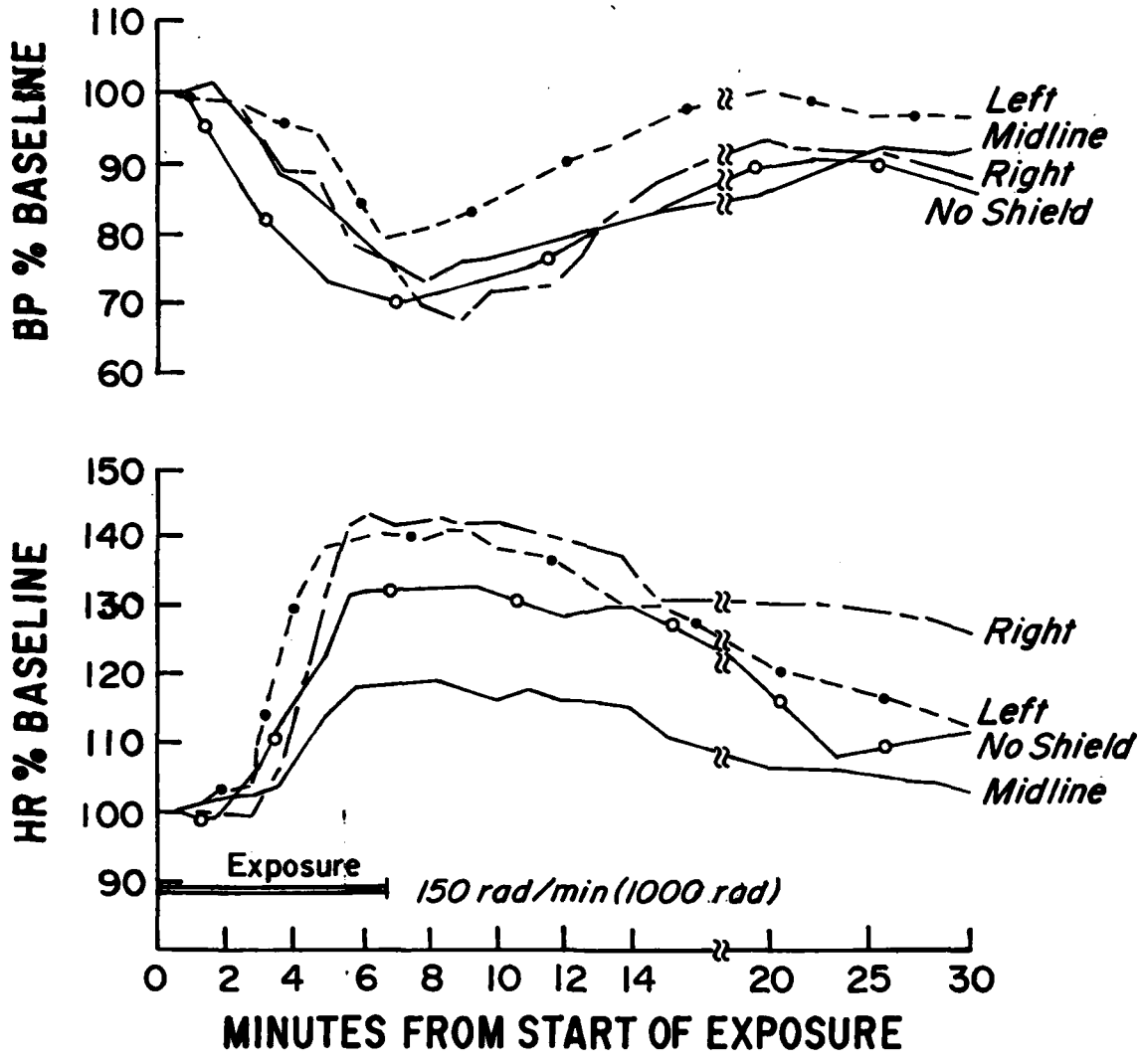

Figure 1. Group Mean Percentages for Blood Pressure (BP) and Heart Rate (HR) Relative to Preradiation Baselines During and After Irradiation for Three Shielding and One Unshielded Groups.

cord and the majority of autonomic trunk ganglia can presumably be ruled out as target organs for the syndrome. At the same time the upper part of the shield employed protected three adjacent sagittal portions of the brain and brain stem, so apparently no identifiable laterality for the hypotensive syndrome exists there. Since about one-third of the head was shielded in each of the shielding groups and no differences in BP or HR were noted relative to the unshielded group, it again appears that the hypotensive response depends primarily on exposure of the trunk,[2,3] since much of the trunk mass was still exposed in all three of the shielding groups.

Since no target organs or discrete systems have been implicated in the early hypotensive syndrome by this or previous studies, we may speculate that the trigger site is diffuse. Such would be consistent with one popular hypothesis of acute radiation injury--the proposition that ionizing radiation directly disables the peripheral vasculature, by some as yet unclear mechanism, perhaps via release of vasoactive substances, e.g., histamine, which cause a loss in vasomotor tone and consequently hypotension.[10-15] Our recent observations[15] have supported the notion that a phasic loss of peripheral resistance accounts for the hypotension. They further suggest that a subsequent

vasoconstriction and reduction in heart output may develop and jeopardize cerebral perfusion and as well, therefore, task performance.

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